Equifem

Drospirenone 2 mg
Estradiol 1 mg

Formula:
Each tablet contains: 2 mg Drospirenone, 1 mg Estradiol (as hemihydrate), and excipients q.s.

Therapeutic action:
Hormone replacement therapy.

Indications:
Treatment of symptoms of estrogen deficit due to natural or surgically produced menopause, such as hot flashes, sleep disturbance, urogenital atrophy and mood changes linked to these alterations. In patients not suffering from vasomotor disturbances, this medication does not act against mood changes or depressive states. ***Equifem*** in combination with other therapies (e.g. adequate calcium supply, physical exercise) is indicated for preventing or slowing bone tissue loss (osteoporosis) in post-menopausal women.

Pharmacological action:
Equifem is a preparation containing estrogen and a progestogen as active ingredients for hormonal replacement during menopause or after surgically induced menopause. The Estradiol/Drospirenone combination has a beneficial effect on the symptoms of menopause and maintains bone mass, reducing the incidence of osteoporosis.

Pharmacodynamics:
Equifem is a combination of a natural estrogen (Estradiol) with Drospirenone, an analogue of Spironolactone, with antimineralocorticoid activity. Drospirenone also possesses antiandrogenic effects.

Pharmacokinetics:
Estradiol is rapidly absorbed in the gastrointestinal tract after oral administration. Maximum plasma concentration is reached 2 to 4 hours after administration. Between 97.5 and 99 % binds to plasma proteins. Around 90 to 95 % is excreted in urine as inactive conjugates and between 5 and 10 % is eliminated in faeces.
Drospirenone has a bioavailability of approximately 76 %. About 97 % binds to serum proteins and it has a half-life of approximately 30 hours. Its metabolites are inactive.

Dosage and method of administration:
Usual dosage is 1 tablet per day. Swallowing the tablets with water is recommended. tablets may be taken with or without food, preferably at the same time every day. Treatment must be continuous and uninterrupted. As soon as one pack is finished, a new one must be started.

Contraindications:
Present, previous or suspected breast carcinoma; estrogen-dependent neoplasias, such as endometrial carcinoma; acute or chronic liver disease, present or previous liver tumours, Dubin-Johnson syndrome, Rotor syndrome, cholestatic jaundice, idiopathic jaundice of pregnancy, intractable pruritis during a previous pregnancy; gestational herpes, porphyria, sickle-cell anemia; pre-existing or present deep vein thrombosis, thrombophlebitis, thromboembolic disorders or history of events that may be linked with past usage of estrogens, cerebrovascular accidents or coronary artery disease; otosclerosis, systemic lupus erythematosus, hard-to-control arterial hypertension, vaginal bleeding of unknown origin; endometriosis; hypersensitivity to any of the ingredients; present or suspected pregnancy, lactation, renal insufficiency, adrenal insufficiency.

Warnings:
Equifem contains 2 mg of Drospirenone which has antimineralocorticoid activity, including the potential to cause hypercalcemia in high-risk patients. Therefore it should not be used in patients with a condition predisposing them to hypercalcemia, such as renal insufficiency, hepatic dysfunction or adrenal insufficiency.
Women who are concomitantly taking drugs that can increase serum potassium should have their plasma potassium levels monitored, especially during the first cycle of treatment. Drugs that increase potassium levels include angiotensin-converting enzyme inhibitors (ACEI), antagonists of angiotensin II receptors, potassium sparing diuretics, heparin, aldosterone antagonists and non-steroid anti-inflammatory drugs (NSAID).

Precautions:
Before commencing estrogen therapy, the patient's full medical and family histories must be taken, and physical and gynecological examinations must be carried out, paying particular attention to arterial blood pressure and to palpation of the breasts and abdomen. If abnormal or irregular vaginal hemorrhaging occurs shortly after the commencement of or during the treatment, a diagnostic biopsy by vacuum aspiration or curettage must be carried out in order to exclude the possibility of uterine cancer. It should be taken into account that the size of uterine leiomyomata (fibroids) may increase. Low doses taken for short periods do not have a measurable effect on this risk. However it is not known at present whether prolonged administration of low doses of estrogens may increase the risk of breast cancer. Consequently, there is a need for special prudence and strict monitoring of women with a family history of breast cancer and patients who present with breast nodules, fibrocystic mastopathy or atypical mammograms. In general, women who take oral hormones should have regular breast monitoring and be taught how to perform breast self-examination.
As a general rule, an annual general and gynecological examination is a requirement for treatment with ***Equifem***. The requisite conditions for hormone replacement therapy must be monitored regularly. Long-term treatment for post-menopausal osteoporosis should be restricted to women who are at high risk for post-menopausal osteoporosis. Known risk factors for osteoporosis are: Caucasian women, early menopause (natural or surgically induced), low body weight, family history, calcium deficiency, smoking, severe immobility, corticosteroid usage, alcohol abuse. Patients treated with antihypertensives or following hormone replacement therapy must have their arterial pressure measured regularly. Patients suffering from epilepsy, migraine, diabetes, asthma, conditions related to high risk of myocardial infarction, cardiac insufficiency, all forms of hepatic function disorder or gallbladder disease, must also be examined closely, because estrogens can exacerbate these conditions by causing water retention. Caution is particularly indicated in cases of migraine, uterine myoma, disorders of lipid metabolism and severe chronic depression. Oral administration of preparations containing estrogens and combinations of estrogens and progestogens may increase the incidence of thromboembolic diseases. This risk is increased in the presence of additional risk factors: smoking, severe obesity, advanced age, arterial hypertension, disturbances of coagulation or of lipid metabolism, diabetes with vascular alterations, varicose veins as well as previous treatments for varicose veins and thrombosis. Cause-effect relationships should be explained to patients. The medication is contraindicated in patients with hepatic or renal insufficiency. There is only limited experience with patients over 65 years of age.

Carcinogenicity:
Carcinogenicity studies in mice treated for 24 months with high doses of Drospirenone showed increased incidence of benign and malignant tumours of the adrenal gland.

Mutagenicity:
Drospirenone was not mutagenic in several in vitro studies.

Pregnancy:
Pregnancy category X. There is evidence of risk to the fetus based on experience in human beings and animals and the risks associated with use of this medicine in pregnant women are much greater than its potential benefits. This medicine is contraindicated for women who are or may become pregnant.

Lactation:
Equifem should not be administered to breast-feeding women.

Drug interactions:
Other medications having effects on ***Equifem*:**
Drugs that induce hepatic enzymes may reduce the effectiveness of ***Equifem***.
Anti-epileptic drugs: Phenobarbital, Phenytoin, Carbamazepine.
Antimicrobial (antibiotic and antiviral) drugs: Rifampicin, Nevirapine, Efavirenz, Ritonavir, Nelfinavir.
Herbal products contained in Hypericum perforatum (St. John's wort) may increase hepatic enzymes (cytochrome P450).

Equifem effects on other drugs:
- Interactions with drugs that potentially increase serum potassium: aldosterone antagonists and potassium-sparing diuretics.

Side effects:
Appearance of the undesirable effects listed under "Precautions" requires immediate suspension of the treatment. The following additional side-effects may occur, especially during the first few months of treatment: Adverse effects on:
Whole body: abdominal pain or inflammation, loss of strength, pain in a limb, back pain, general malaise.
Cardiovascular system: arterial hypertension, palpitations, deep vein thrombosis, superficial thrombophlebitis, venous dilation.
Digestive system: nausea, increased appetite, increased hepatic enzyme levels.
Metabolism and nutrition: edema, dyslipidemia.
Musculoskeletal system: muscle cramps, joint pain.

Nervous system: occasionally headaches, insomnia, migraine, vertigo and depressive states may occur.
Respiratory system: dyspnea.
Skin and related tissues: hair loss, hirsutism.
Genitourinary system: enlargement of benign uterine tumours, vulvovaginitis, leukorrhea, dysmenorrhea, urinary tract inflammation, urinary incontinence.

Overdose:
No cases of overdose have been recorded. The most likely symptoms of acute overdose are nausea and vomiting. Treatment is symptomatic.

Presentation:
Blister pack containing 28 coated tablets.
Store at room temperature (15-30oC).
Keep out of the reach of children.